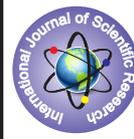


A BRIEF REVIEW OF MANAGEMENT OF CARCINOMA LARYNX



Oncology

KEYWORDS: - Larynx, Surgery, Radiotherapy

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ABSTRACT

Carcinoma larynx constitutes about 25% of all Head and Neck tumors. Incidence of supraglottic and glottic cancers are more common than sub-glottic. Histopathological confirmation is required for establishing the diagnosis. Imaging helps in knowing the loco-regional extent of the disease. Treatment strategies focus on voice preservation besides improving loco-regional control and survival. For early glottic and supraglottic tumors both surgery and radiotherapy (RT) are equally effective. For advanced glottic and supraglottic tumors concurrent chemoradiation (CT-RT) is usually preferred over surgery for organ preservation. Subglottic tumors are rare, surgery followed by post-operative RT or concurrent CT-RT both are treatment options.

INVESTIGATIONS

First complete medical history should be taken and proper physical examination should be done.

Examination is done by laryngoscope (direct and indirect) which is an out patient door procedure. Patients with laryngeal cancers also have higher risk of other cancers in the head and neck region, so the oral cavity, oropharynx, nasopharynx and hypopharynx should also be examined carefully. B/L neck should be examined for any metastatic lymphadenopathy.

Panendoscopy (combination of laryngoscope, esophagoscope and bronchoscope) could be used to look for tumors in larynx and hypopharynx.

Endoscopic biopsy from suspicious lesion and Fine needle aspiration cytology from secondary nodal sites are done for histopathological confirmation. Chest X-ray is required to exclude lung metastasis. Contrast-enhanced computed tomography (CECT) scan or Magnetic resonance imaging (MRI) could be used to assess the loco-regional extent of the disease, however MRI is more sensitive but less specific than CT scan for laryngeal cartilage invasion. Positron emission tomography (PET) scan might be helpful in assessing metastatic disease or recurrence after treatment.

TREATMENT

Most of the cases of verrucous carcinoma of vocal cords present in early stage. Treatment of verrucous carcinoma of vocal cords with radiotherapy (RT) is controversial as some studies have shown that it is less radioresponsive and RT leads to development of anaplastic transformation while some studies found RT effective (1). In one-third of cases salvage treatment in form of surgery is required due to local failure after RT. Five- year disease specific survival is 97% (2). Treatment depends upon disease extent. Small tumours are managed surgically (excision or partial laryngectomy) while in large tumors requiring total laryngectomy, RT should be considered. Chemotherapy can be added in aggressive cases.

Treatment of carcinoma-in-situ (CIS) varies from post- biopsy observation, cordectomy, vocal cord stripping and open partial laryngectomy to primary radiation. Post-biopsy observation should be done with caution as the disease may progress to invasive form. Primary RT is an effective treatment for carcinoma in situ of larynx. Local control rate with primary RT, laser resection and vocal cord stripping are 87%, 83% and 72% respectively (3). Radiation is best modality for recurrence, for more diffuse primary lesions and for those in whom limited surgery is not beneficial. RT dose of 60 Gy is effective, however higher doses can be given because about one-third of patients might have unrecognized invasive disease.

For management of early stage glottic tumours (T1- T2, N0) either voice-preserving surgery i.e. partial laryngectomy or irradiation is advised but some other modalities like laser excision can also be tried

for T₁ glottic tumors. However, either surgery or voice-preserving surgery which one is better is still unknown. There are no randomized trials but multiple studies have suggested that no one modality could be proven superior over other with regard to all treatment goals (4,5,6)

One of the important factor in selecting the treatment for individual patient is the anticipated voice quality after therapy while other factors are location and extent of tumor, characteristic growth of tumor, vocal cord mobility, histology, general medical condition of the patient, patients affordability for surgery and preference of the treating surgical and radiation oncologists.

Yamazaki et al conducted a randomized trial and compared 2 Gy per fraction versus 2.25 Gy per fraction in the treatment of stage 1 glottic cancer. In this study, smaller tumors were given slightly lower dose (56.25 Gy in 2.25 Gy fractions or 60 Gy in 2 Gy fractions) than larger tumors (63 Gy in 2.25 Gy fractions or 66 Gy in 2 Gy fractions). Larger fraction size increased local control from 77% to 92%, corroborating the previously published retrospective series that suggested that larger fraction size improves local control. On multivariate analysis, treatment arm was the only significant independent prognostic factor with an odds ratio of 3.38. This study established hypofractionation with 2.25 Gy as a standard fractionation schedule for T1-N0 glottic cancer (7).

Although the radiotherapy techniques and doses may vary, but a standard course of radiation for glottic tumors usually consists of a total 60-70 Gy given in single daily fraction over 6 weeks.

With RT, there are several advantages mainly voice preservation in 80-90% of the cases ,avoidance of surgery and subsequent hospitalization whereas disadvantages are mainly the long treatment course, early and late side effects of radiation (mucositis ,dermatitis ,xerostomia ,dysphagia/odynophagia weight loss and hypothyroidism, carotid artery stenosis, pharyngeal strictures, osteoradionecrosis of the mandible, radiation induced secondary malignancy).

More recently in a study done by the Radiation Therapy Oncology Group (RTOG), which compared concurrent chemoradiation therapy, induction chemotherapy followed by radiation therapy and radiation therapy alone showed that laryngeal preservation at 2 year was 88%, 75% and 70% respectively.

Factors that contributes to the outcome of treatment are subglottic extension , male gender and advanced histopathological findings however paraglottic extension is associated with increased tumor volume but it is not associated with increased local failure .

Due to additional involvement of neck lymphatics, clinical presentation of supraglottic carcinoma is different from that of glottic carcinoma and in maximum patients cervical lymph nodes

are involved. Endoscopic laser resection, open-partial supraglottic laryngectomy and radiation are all considered standard treatment options for early supraglottic carcinomas. Choice of treatment depends upon location and extent of tumor, general condition of patient and associated comorbidity. In many cases even after partial laryngectomy adjuvant RT is required. Concurrent CT-RT is also an option for large T2 lesions. In such cases now it is recommended to add cisplatin with RT or surgery can also be done along with adjuvant RT. Patients having failure after radical RT could be salvaged with surgery.

Bilateral arytenoid involvement, extension into the glottic area, invasion of the thyroid or cricoid cartilage, involvement of the postcricoid region, arytenoid fixation, involvement of the apex of the pyriform sinus, impaired vocal cord mobility and extensive involvement of the base of the tongue are some contraindications for supraglottic laryngectomy. Prognosis of supraglottic carcinoma is more compromised than that of glottic carcinoma. Orus et al have showed better initial local control with partial laryngectomy as compared to RT but, with salvage surgery, both resulted in same local control of 90% for T₁- and T₂-N₀ supraglottic tumors (8).

Therapeutic approaches for locally advanced (stage III and IV) glottic and supraglottic cancer are same. Concurrent chemoradiation is considered as standard of care even in resectable cases as it is better than RT alone and offers advantage of laryngeal preservation (9,10). Total laryngectomy should be considered for patients having T₄ lesions with extensive cartilage involvement or as salvage treatment after local failure to chemoradiation. T3 and T4 cancers have a higher risk of metastasis to nearby lymph nodes in the neck as compared to early-stage cancers, so it is advised to do neck dissection in all cases if surgery is done.

For selective T₃ and T₄ lesions, larynx-preserving surgery could be considered alternative to chemoradiation. However, postoperative radiation might be needed in such patients. There is no prospective randomized trial comparing primary surgery and concurrent chemoradiation exclusively in advanced carcinoma larynx. The prognosis of advanced carcinoma larynx is poorer as compared to early stage disease and long-term survival varies from 30% to 60% (11). Stage III-IV disease patients who could not be given concurrent chemotherapy should be treated with hyperfractionated or accelerated hyperfractionated RT. A phase-III RTOG randomized trial demonstrated that hyperfractionation and accelerated fractionation with concomitant boost are associated with better local control and disease-free survival as compared to RT with standard fractionation for locally advanced head and neck cancers (12).

RTOG 91-11 conducted a phase III randomized trial in patients of stage III and IV nonmetastatic, squamous cell carcinoma of the glottic and supraglottic larynx with three approaches: RT alone, concurrent CT-RT, induction CT and local treatment based on response. In this trial it was concluded that cisplatin based concurrent chemoradiation was beneficial over others (13). Cetuximab could be considered for patients in whom cisplatin could not be given.

Regarding induction chemotherapy, it has been shown that taxane added to platin and 5-FU is superior to platin and 5-FU alone in advanced head and neck cancer.

Postoperative chemoradiation therapy has shown to be associated with better locoregional control and survival benefit compared with radiation alone in patients who have extracapsular extension (ECE) of a lymph node or positive surgical margins (14).

Primary carcinoma of subglottis is rare and usually presents at advanced stage (15). Surgery followed by postoperative RT is considered as standard of care. RT alone is considered for early lesions, for patients reluctant to surgery or not suitable for surgery

(due to any comorbidity) with 5-year survival approaching 50%. (16).

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